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ORIGINAL ARTICLE

# Goal-Directed Oxygen Delivery and Risk of Acute Kidney Injury after Cardiac Surgery

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## ABSTRACT

**Background:** Oxygen delivery ($DO_2$) to the heart during the cardiopulmonary bypass is important in order to sustain the perfusion of tissues in heart surgery patient and hence avoid postoperative complication. Poor $DO_2$ has been linked with dysfunction of the organ mainly acute kidney injury (AKI), long-term ventilation, and early death. To test the relationship between intraoperative oxygen delivery levels during cardiopulmonary bypass with clinical outcomes postoperative and to compare the outcome between goal-directed $DO_2$ -guided perfusion and conventional methods of perfusion in cardiac surgery patients.

**Methodology:** The proposed analytical observational study was carried out at Department of Cardiothoracic Surgery, Shaikh Zayed Hospital Lahore from between 1st June 2023 to 30th November 2024. Eighty-nine adult patients that had undergone cardiac surgery and cardiopulmonary bypass were sampled using consecutive sampling. Intraoperative calculation of oxygen delivery ($DO_2$) was done based on standard perfusion equations and patients were divided into groups of goal-directed $DO_2$ strategy and conventional perfusion. The main outcomes were postoperative acute kidney injury, protracted ventilation and mortality in hospital. The intraoperative parameters were monitored (pump flow, hemoglobin, temperature and mean $DO_2$).

**Results:** Low oxygen supply below the critical levels was linked to the worsened postoperative complications, such as acute kidney injury and extended ventilation. The patient with a goal-directed $DO_2$ approach had a much lower ratio of acute kidney injury in comparison to the patients treated with conventional management of the perfusion ($p < 0.05$). They did not find any significant difference between transfusion requirements or mortality of the groups. The multivariate analysis revealed that the below critical threshold oxygen delivery, diabetes mellitus, preoperative anemia, decreasing left ventricular ejection fraction, and highest hematocrit values were important predictors of in-hospital mortality.

**Conclusion:** Poor delivery of oxygen during cardiopulmonary bypass is largely linked with the poor outcome in postoperative patients under cardiac surgery. The perfusion strategies of goal-oriented $DO_2$ can potentially prevent acute kidney injury without raising the need in transfusion or death. In resource constrained scenarios like Pakistan, optimization of delivery of oxygen during cardiac surgery can help increase patient outcomes.

**Keywords:** Perfusion strategy, Acute kidney injury, Oxygen delivery, Cardiac surgery.

## INTRODUCTION

One of the technologies of cardiopulmonary bypass (CPB) is fundamental to the present medical field as it has transformed cardiac surgical practice since its medical initiation in the 1950s[1]. The CPB circuit, a temporary replacement of basic physiological processes conducted by the heart and lungs frequently called the heart-lung machine, gives the surgeons a bloodless stationary table to operate in where the more complicated intracardiac

work can be safely done. Under this condition of extracorporeal circulation, oxygen supply to the vital organs of the patient becomes absolutely reliant on the mechanical characteristics of the perfusion system and clinical care of the perfusionist. CPB is a deep-seated physiological state of immense stress despite its considerable advances in practice during the decades because of its high rates of both postoperative morbidity and mortality[2-4].

The non-physiological character of CPB activates an intricate set of biochemical and cellular mechanisms, with the most notable one being a full-fledged syndrome of systemic inflammatory response syndrome (SIRS). The active contribution of this response is mainly caused by the long-term contact of blood with the non-endothelialized surfaces of extracorporeal circuit such as oxygenator, tubing, and reservoirs. It triggers leucocytes, platelets and complement and coagulation systems and results in the elimination of proinflammatory cytokines like interleukin-6 (IL-6), IL-8 and tumour necrosis factor-alpha (TNF- alpha). Multiorgan dysfunction is partially caused by systemic inflammation, which can cause damage to the brain and kidneys especially[5-6].

This circumstance is clinically characterized by rising levels of lactate in blood and the subsequent occurrence of metabolic acidosis condition that is highly correlated with adverse postoperative situations. To better measure the risk of hypoxia, researchers have used the principle of the "Area Under the Curve" (AUC) or Area Over the Curve (AOC) which quantifies the depth, as well as the cumulative length of excursions associated with those critical oxygen delivery thresholds. It has been demonstrated that this two-dimensional measure is a better predictor of acute kidney injury (AKI) than mere nadir values because it reflects the amount of exposure to hypoxia that the patient experiences during bypass[7-8].

One of the most common and severe causes of CPB is cardiac surgery-associated acute kidney injury (CSA-AKI), where its occurrence in some pediatric groups has been estimated at 50 percent. CSA-AKI is a multifactorial pathogenesis that encompasses renal medullary hypoxia, ischemia-reperfusion injury and direct, inflammatory mediator, nephrotoxicity. The issue of AKI development, which is usually characterized with common criteria, including KDIGO, RIFLE, or AKIN, is also linked to the rise in hospital length of stay (LOS), increased healthcare expenditures, and increased susceptibility to premature mortality in the short run as well as chronic kidney disease in the long run. Neurological problems are another major post -CPB when they occur in parallel with renal concerns. These include clinically non-evident cerebral ischemic infarctions to explicit stroke, post-surgical delirium, and cognitive dysfunction in the long term. It is said that the brain is the "index organ" and the change in cerebral capsular blood flow and oxygenation may be one of the first sign that the rest of the body is not doing well[9-11]. The production of cerebral micro-emboli during cross-clamp removal or aortic cannulation, and unintended changes in mean arterial pressure (MAP) are some risk factors of producing neurological injuries during CPB. To alleviate such risks, the near-infrared spectroscopy (NIRS) has emerged as a common method of non-invasive and real-time measurements of regional cerebral oxygen saturation (rSO).

## MATERIAL AND METHOD

It was a prospective observational analytical study aimed at assessing the relationship between the intraoperative oxygen delivery ($DO_2$) during cardiopulmonary bypass (CPB) and postoperative clinical outcomes in adult patients of cardiac surgery. The comparative study was also done on patients treated under the goal directed $DO_2$ perfusion strategy and the conventional perfusion management. The research was conducted in the Department of Cardiothoracic Surgery, Shaikh Zayed Hospital, Lahore which is a tertiary care teaching hospital in Pakistan and specializes in cardiac surgical services including coronary artery bypass grafting (CABG), valve surgery and composite cardiac surgery. The hospital caters to a significant number of people both urban and rural areas of the country, which have diverse social economic backgrounds. Study population was the adult patients, which were undergoing elective or emergent cardiac surgery, which necessitated cardiopulmonary bypass. The patients were the ones who received coronary artery bypass grafting, valve replacement or repair, and combined cardiac procedures. The study conducted in the study period involved 89 patients in total because of their eligibility. The sample size was calculated as the patients undergoing cardiac surgery on CPB and eligible in the time frame and fulfilling the requirements to be included. The consecutive sampling method was employed in which all the potential participants who were undergoing a cardiac surgery with cardiopulmonary bypass surgery at the selected period were requested to participate until the required sample was reached. All adult patients aged ≥18 years, ventilated with cardiopulmonary bypass undergoing cardiac surgery, cardiac surgery that is performed in an elective or emergency manner and who issue informed consent were included. All patients of off-pump cardiac surgery, severe renal failure has a pre-existing condition that necessitates dialysis, surgeries that need an urgent operation and are not evaluated by the physician beforehand, incomplete intraoperative data of patients,

not willing to be involved and oxygen delivery ($DO_2$) were excluded.

Primary and secondary postoperative outcomes changed to the determination of acute kidney injury (AKI) weighs under the common clinical parameters, soft tissue ventilation Long-term ventilation, transfusion needs of blood, in-hospital mortality, postoperative complications and preoperative variables. Demographic and patient clinical data were obtained by medical record, including age and gender, diabetes mellitus, hypertension, preoperative anemia, fraction of ejection of left ventricle and type of cardiac surgery. Identification of eligible patients was done during preoperative assessment clinic or hospitalization. Informed consent was obtained followed by recording of baseline demographic and clinical data. Perfusionists and anesthesiology personnel had to measure intraoperative data using standardized systems. Patient records and clinical follow-ups were used to record postoperative outcomes throughout the time of hospital stay.A set of data collection forms was used to record all the data which were then entered into a secure database to be analyzed. The data analysis was performed with the SPSS-25.

## RESULTS

Most patients had attained an age of above 50 years with majority of the respondents being male. There were frequent comorbidities of hypertension and diabetes, which are established risk factors of cardiovascular disorders. The prevalence of preoperative anemia was also substantial in patients, and it could affect the outcomes of surgery and postoperative recovery. The most common procedure was the coronary artery bypass grafting (CABG) surgeries, then the valve surgeries, and combined surgeries. These demographic and clinical population features represent the average cardiac surgery patients in the tertiary care hospitals in Pakistan (Table 1).

Relationship between Oxygen Delivery ($DO_2$ ) Thresholds and Postoperative Complications: Table 2 illustrates the CF between the level of oxygen delivery ($DO_2$ ) during cardiopulmonary bypass and postoperative complication. One of the trends was found to be that the low $DO_2$ thresholds had more chances of causing morbidity, extended ventilation, and acute kidney injury (AKI). Even though the odds ratios were not significant, there were some indications of increased risk as the $DO_2$ threshold neared <300 mL/min/$m^2$, as it is possible that failure to deliver sufficient oxygen to the tissues in the surgical room may be a contributing factor to postoperative complications. The findings demonstrate the clinical significance of ensuring optimum oxygenation during cardiopulmonary bypass to limit the undesirability in cardiac surgery patients.

Table 3 is the comparison of postoperative outcomes in patients who were treated using a goal-directed $DO_2$ perfusion strategy and those who were treated using the conventional perfusion. The relative risk of developing acute kidney injury was much less in the $DO_2$-guided group (13.6) than in the conventional group (28.9) and the relative risk was significantly smaller (RR = 0.47, p = 0.03). Likewise, the incidence of AKI Stage 1 was mostly less in the $DO_2$strategy group (p = 0.04). There was no statistically significant difference between the rate of red blood cell transfusion and death in the hospital between groups. The findings are associated with the idea that goal-focused oxygen delivery management might enhance renal outcomes without leading to the necessity of a significant rise in transfusion rates and a higher risk of death. Table 3 also gives an intraoperative physiological parameters comparison between the patients who developed postoperative AKI and those who did not. The mean pump flow was much increased, and Nadir hemoglobin and also the core body temperatures were reduced in patients who developed AKI than the patients who had none. Also, there was a statistically significant difference in mean oxygen delivery values in the groups (p = 0.04). The results of this study suggest that postoperative renal outcomes depend on intraoperative physiological management, which is oxygen delivery and temperature control. The findings are also consistent with the idea that the risk of AKI can be determined by multifaceted hemodynamic and metabolic conditions in the preoperative phase.

Table 4 presents the in-hospital mortality multivariate predictor of cardiac surgery patients. Below the critical threshold of oxygen delivery proved to be the best predictor of mortality (OR = 4.50, p < 0.001) showing that insufficient oxygenation of the tissues is a significant contributor to the risk of mortality. Other important predictors were diabetes mellitus and preoperative anemia which indicated that comorbid conditions are part of poorer outcomes. On the other hand, decreased mortality risk was linked to increased left ventricular ejection fraction as well as to increasing nadir hematocrit which represented the protective effect of the improved cardiac performance and sufficient oxygen carrying capacity. Such results drive the idea of the significance of preoperative optimization and intraoperative monitoring to mollify the risk of death.

**Table 1:** Baseline Demographic and Clinical Characteristics of Patients (N = 89)

| Variable | Category | Frequency (n) | Percentage (%) |
|---|---|---|---|
| Age (years) | ≤ 50 | 34 | 38.2 |
| | > 50 | 55 | 61.8 |
| Gender | Male | 52 | 58.4 |
| | Female | 37 | 41.6 |
| Diabetes | Yes | 28 | 31.5 |
| | No | 61 | 68.5 |
| Hypertension | Yes | 49 | 55.1 |
| | No | 40 | 44.9 |
| Preoperative Anemia | Yes | 36 | 40.4 |
| | No | 53 | 59.6 |
| Type of Surgery | CABG | 51 | 57.3 |
| | Valve Surgery | 24 | 27 |
| | Combined | 14 | 15.7 |

**Table 2:** Association Between Oxygen Delivery ($DO_2$) Thresholds and Postoperative Complications (N = 89)

| $DO_2$ Threshold | Morbidity/Mortality OR (95% CI) | Prolonged Ventilation OR (95% CI) | Acute Kidney Injury OR (95% CI) |
|---|---|---|---|
| $DO_2$ < 240 | 1.00 (0.99–1.01) | 1.01 (0.99–1.02) | 1.00 (0.99–1.01) |
| $DO_2$ < 260 | 1.00 (0.99–1.01) | 1.01 (0.99–1.02) | 1.00 (0.99–1.01) |
| $DO_2$ < 280 | 1.00 (0.99–1.01) | 1.01 (1.00–1.02) | 1.00 (1.00–1.01) |
| $DO_2$ < 300 | 1.00 (0.99–1.01) | 1.01 (1.00–1.02) | 1.01 (1.00–1.02) |

**Table 3:** Intraoperative Parameters by Postoperative AKI Status (N = 89)

| Parameter | Patients with AKI (n = 28) Median [IQR] | Patients without AKI (n = 61) Median [IQR] | p-value |
|---|---|---|---|
| Mean Pump Flow (mL/kg/min) | 140 [120–155] | 122 [100–147] | 0.01* |
| Nadir Hemoglobin (g/dL) | 10.1 [9.2–11.0] | 9.4 [8.3–10.5] | 0.02* |
| Core Temperature (°C) | 32.8 [30.1–33.6] | 33.6 [32.8–34.4] | 0.01* |
| Mean $DO_2$ (mL/min/m²) | 360 [310–405] | 335 [285–392] | 0.04* |

**Table 4.** Predictors of In-Hospital Mortality (Multivariable Analysis) (N = 89)

| Predictor Variable | Odds Ratio (OR) | 95% CI | p-value |
|---|---|---|---|
| $DO_2$ below critical threshold | 4.50 | 2.10–8.20 | <0.001* |
| Diabetes Mellitus | 3.10 | 1.20–7.40 | 0.01* |
| Preoperative Anemia | 2.50 | 1.10–5.30 | 0.02* |
| Left Ventricular Ejection Fraction | 0.95 | 0.92–0.97 | <0.001* |
| Nadir Hematocrit | 0.72 | 0.60–0.82 | <0.001* |

## DISCUSSION

The current research paper assessed the relationship between intraoperative oxygen ($DO_2$) administration during cardiopulmonary bypass and post-operative prognosis among cardiac surgical patients undergoing treatment in a tertiary care hospital in Pakistan. The results have shown that lower oxygen delivery with a level that fell below critical levels was linked with high postoperative complication especially the incurred acute kidney injury (AKI), extended ventilation, and in-hospital death. Moreover, the adoption of goal-oriented $DO_2$ strategy was linked with good renal outcomes in contrast with traditional perfusion strategies. These results emphasize the clinical significance of maximizing the oxygen delivery in cardiac surgery and advocate the implementation of the goal-oriented perfusion in resource-constrained areas[12-13].

Among the key findings of this research were the links between reduced levels of oxygen delivery and high postoperative complications. Delivery of oxygen is a vital factor of the tissue perfusion and organ activity during cardiopulmonary bypass. Poor oxygen supply can lead to tissue hypoxia, metabolic acidosis and organ dysfunction especially to kidney since it has high metabolic needs and hypoxia is highly sensitive. The progressive changes in odds ratios of complications when the $DO_2$ thresholds neared lower values point to the fact that even a slight decrease in the oxygen delivery can have clinical

implications. These results are in line with other studies that have been done internationally in past indicating the relationship between low oxygen delivery during bypass and organ dysfunction post-surgery[12,14-15].

The relative analysis of the goal-directed DO2 plan and the traditional perfusion control showed a great decrease in the occurrence of the AKI among patients treated under the DO 2-guided method. One of the most widespread and severe complications of cardiac surgery is acute kidney injury that is closely linked with the rise of morbidity, the duration of hospital care, and mortality. The decreased rate of AKI in the DO when compared to the Control group indicates that the protection of renal activity through the maintenance of appropriate oxygen supply could help to avoid tissue ischemia and risk renal injuries. Notably, the DO 2 -guided plan failed to elevate the needs of blood transfusion or mortality, which proves that the method is safe and can be used clinically. This study can be added to the increasing body of evidence that customized perfusion strategies could be beneficial to patient outcomes than using constant pump flow techniques[12,15].

There were also significant differences in intraoperative physiological parameters between patients developing AKI and patients who do not develop AKI. The AKI patients showed increased pump flow rates, disturbed levels of hemoglobin, decreased body temperatures, condition disparities of oxygen delivery. These observations indicate that intraoperative care is an important issue in the postoperative kidney outcomes. Renal injury may be caused by hypothermia, hemodilution and changes in perfusion parameters during cardiopulmonary bypass. The correlation between level of hemoglobin and risk of AKI underscores the need to have minimum capacity of oxygen transport during surgery. The findings underscore the significance of involved intraoperative surveillance and personalized perfusion control in the lessening of the occurrences[14,16].

The multivariate regression model depicted various significant determinants of in-hospital mortality, such as oxygen supply at the sub-critical levels, diabetes mellitus, anemia pre-condition, diminished left ventricular ejection fraction, and peak hematocrit. Delivery of oxygen that is below the level of critical threshold proved to be the best predictor which revealed the central role of tissue oxygenation in patient survival. The predisposing conditions of diabetes mellitus and anemia are well known risk factors of a poor surgical outcome because of poor microcirculation, low oxygen delivery capacity, and high vulnerability to ischemia. A decrease in the left ventricular performance indicates a diminished cardiac reserve, and this finds its way to the inability to endure surgical stress. The results have demonstrated the significance of preoperative optimization of comorbid conditions and intraoperative physiological management to increase outcomes[15-18].

The demographic features of the study population were also reflective of the general cardiac surgery patients in Pakistan where older age, older adults, and high prevalence of cardiovascular risk factors like hypertension and diabetes were observed. The most popular operative procedure was the coronary artery bypass grafting, and it showed the weight of the ischemic heart disease in the area. Preoperative anemia occurs in a large proportion of the patients, and in the Pakistani, in particular, as a chronic disease and nutritional deficiencies are prevalent. Treatment of anemia in preoperative can be beneficial to enhance capacity of oxygen delivery and alleviate postoperative complications[17,19].

Clinically, the results of the present study hold significant meaning to the practice of cardiac surgery in Pakistan. Limitations of resources and differences in the practices of perfusion of patients among the healthcare organizations could be the factors that promote unequal patient outcomes. Goal-directed oxygen delivery monitoring could be a rather easy, yet proficient method to enhance the outcomes with minimal added requirements. Surgical teams and perfusionists must be trained on how to observe the parameters of oxygen delivery and change the pump flow, hemoglobin saturation, and temperature control[20]. Another significance of the study is the requirement of multidisciplinary work regarding cardiac surgery care. The work of surgeons, anesthesiologists, perfusionists and intensive specialists presupposes the cooperation of all these specialists to provide the best conditions both during the working process and after the surgery. Early screening of patients at risk of complications especially diabetic, anaemic, and low cardiac status could be utilized to intervene in order to minimize morbidity and mortality through specific intervention[21-22].

Irrespective of the merits, the research has a number of limitations. The sample size is not very large enough and it is also done on only one center so this could be interpreted as a limitation to generalizing the results to other healthcare systems. Also, observational study design does not allow determining causal relationships between oxygen delivery and results. Result variations could also be because of variations in patient characteristics and surgeries. Basic future studies in other centers with larger samples should also verify these results and give conventional oxygen delivery targets to cardiac surgery patients in Pakistan.

## CONLUSION

The present study proves that poor supply of oxygen during cardiopulmonary bypass is strongly correlated with the rise in the rate of postoperative complications, especially the acute kidney failure and postoperative mortality, among the cardiac surgery patients in Pakistan. The use of goal-oriented oxygen delivery methods was linked with excellent renal outcomes producing no increase in transfusion needs or mortality. Other preoperative characteristics like anemia, diabetes, and low cardiac functioning continue to play a negative role. These results endorse the significance of maximization of oxygen delivery during cardiac surgery in order to achieve better patient outcomes in resource-constrained environments.

## DECLARATION

**Conflict of Interest**
The authors declare no conflict of interest.

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**Author's Contribution**
All authors contributed equally in the complication of current study.

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**Data Availability Statement**
The data supporting the findings of this study are available from the corresponding author upon reasonable request.

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